

## REMARKS

Claims 1, 4, 7, and 8 are pending and under examination in the present application.

### **The October 11, 2006 Office Action**

#### Examiner's Rejection under 35 U.S.C. §112, first paragraph

Claim 8 was rejected under 35 U.S.C. §112, first paragraph, as allegedly lacking adequate written description. According to the Examiner, the specification lacks sufficient support for comparing survival time between a subject who is homozygous for the CCR5 delta 32 mutation and a subject who is heterozygous for the mutation. According to the Examiner, the specification provides only for a comparison of subjects homozygous or heterozygous for the deletion versus those lacking the deletion (i.e., homozygous for no deletion mutation). The Examiner points to the data presented in the tables and figures to support his position.

In response, Applicants respectfully traverse the Examiner's rejection. Claim 8 does not represent new matter as the Examiner alleges. The Examiner's attention is again directed to the disclosure at pages 7-10 of the specification. While the data presented emphasizes the comparison between those individuals having the deletion (either homozygous or heterozygous) versus those not having the deletion, Applicants maintain that one of ordinary skill in the art would recognize from the disclosure (including Table 1) that a subject who is homozygous for the CCR5 delta 32 deletion mutation would be expected to have a shorter survival time than a subject who is heterozygous for the deletion, and thus the ordinarily skilled artisan would conclude that the inventors were indeed in possession of the invention defined by claim 8.

Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of claim 8 under 35 U.S.C. §112, first paragraph.

Examiner's rejections Under 35 U.S.C. §112, first paragraph—enablement

Claims 1, 4, and 8 were rejected under 35 U.S.C. §112, first paragraph, as allegedly lacking full enablement. The Examiner's complete rationale is set forth at pages 3-9 of the Office Action. The Examiner has acknowledged that the specification is enabling for a method for predicting survival time in human subjects having MS and the CCR5 delta 32 mutation versus those having MS but not the mutation, (wherein those having the mutation have a reduced survival time), but, in the Examiner's view, the specification does not enable a method in which a comparison is made between those heterozygous for the mutation and those homozygous for the mutation (as similarly noted in connection with the written description rejection above). Thus, the Examiner appears to be acknowledging enablement at least for the subject matter of pending claim 7.

In response, Applicants respectfully traverse the Examiner's rejection. For reasons similar to those presented above in connection with the written description rejection, Applicants believe that one of ordinary skill in the art would clearly recognize how to make and use the claimed invention without the need to resort to undue experimentation. One of ordinary skill would further understand, based on the present disclosure and knowledge in the art, that a subject who is homozygous for the CCR5 delta 32 deletion mutation would be expected to have a shorter survival time than a subject who is heterozygous for the deletion. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejections of claims 1, 4, and 8 under

35 U.S.C. §112, first paragraph.

Examiner's Claim rejections under 35 U.S.C. §103

The Examiner also rejected claims 1 and 7 as allegedly being obvious under 35 U.S.C. §103(a) over Barcellos, et al., in view of Midgard, et al., for the reasons previously set forth. Similarly, claim 4 was again rejected as being obvious over Barcellos, in view of Midgard, and further in view of Cohen, et al (U.S. Pat. No. 6,265,546). The Examiner's full rationale is set forth at pages 10-13 of the Office Action.

In rejecting the claims, the Examiner has repeated his assertions that Barcellos teaches that age of onset of MS was approximately 3 years later in patients carrying the CCR5 delta 32 deletion, while again acknowledging, however, that Barcellos does not specifically teach that the CCR5 delta 32 deletion correlates to a reduced survival time in subjects having MS versus subjects having MS who do not possess the deletion. The Examiner again has asserted that Midgard, et al. teaches that the shortest survival is in patients with a high age of onset. The Examiner has maintained his position that it would have been obvious for one of ordinary skill in the art to have combined the method and results of Barcellos with the teachings of Midgard to arrive at the conclusion that the presence of the CCR5 delta 32 deletion mutation in a subject with MS is predictive of a shorter survival time versus a subject that does not possess the mutation. The Examiner again has relied on the Cohen reference for its general teaching that whole blood is a useful source of DNA for genotyping analysis.

In response, Applicants respectfully traverse the Examiner's rejection. Applicants continue to believe the Examiner's analysis is flawed. As stated previously, the Examiner's

position necessarily relies first on a conclusion that there is a link between the presence of the mutation in an MS patient and a later age of onset of the disease (as allegedly established by Barcellos), and second, that a later age of onset of the disease correlates with a shorter survival time (as allegedly established by Midgard). Applicants believe, for the reasons set forth in detail previously, that the state of the art (including the references the Examiner has noted in his response to Applicants' arguments) does not reliably support the conclusion at which the Examiner has arrived. Specifically, the Examiner's ultimate conclusion that presence of the mutation correlates with shorter survival time cannot be supported unless the first link in the above chain is established in the art. The art of record, however, establishes no such link. Applicants reiterate that the Examiner himself acknowledged in a previous enablement rejection that the art is unclear in this regard. Specifically, the Examiner stated:

The prior art specific to the CCR5 delta 32 deletion mutation and relative time of survival also indicates the unpredictability of using the presence of the CCR5 delta 32 deletion as an indicator of a shorter relative time of survival. Sellebjerg et al (2000) (as cited in the IDS) teaches an analysis of the CCR5 delta 32 mutation as it correlates to several parameters of disease course in subjects with MS. Sellebjerg et al teaches that the age of onset of disease is lower in patients carrying the delta 32 deletion mutation of the CCR5 gene than in the remaining patients (p.100-Results 3.1 *CCR5 Δ32 in patients and control subjects*). . . . Midgard et al teaches that the shortest survival is in patients with a high age at onset (p.418 - Results; table 1). Taken together, these references would indicate that the delta 32 deletion mutation of the CCR5 gene is indicative of a longer relative survival time. (Underlining added).

Thus, the Examiner's own words acknowledge that there is prior art which, if considered in combination with the art cited in the obviousness rejection would cast doubt on the very


conclusions relied on to sustain the rejection. The present specification in fact also refers to this failure in the art to establish a reliable correlation between presence of the mutation and age of onset of the disease. Paragraph [0009], for example, notes the same inconsistent teachings of Sellebjerg and Midgard to which the Examiner referred, as well as the teachings from a third reference, Bennetts, which offers yet another possible alternative, i.e., that presence of the mutation makes no difference. Thus, because one of ordinary skill in the art could not have believed with any reasonable degree of certainty that presence of the mutation correlates with age of onset, one then could not reasonably have reached the conclusion that the presence of the mutation correlates with survival time. It is the Applicants' invention that has established this link, thereby overcoming the uncertainty that was present in the art at the time of the invention. For at least these reasons, Applicants' claims are not rendered obvious by the cited art. Accordingly, Applicants respectfully request reconsideration and withdrawal of the Examiner's rejection under 35 U.S.C. §103.

In view of the above remarks, Applicants believe all of the Examiner's rejections set forth in the October 11, 2006 Final Office Action have been fully overcome and the application is in condition for allowance. The Examiner is invited to telephone the undersigned if it is deemed to expedite allowance of the subject application.

Respectfully submitted,

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